The Science Behind the Academy for Eating Disorders' Nine Truths About Eating Disorders

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ABSTRACT

Objective: In 2015, the Academy for Eating Disorders (AED) closely collaborated with international patient, advocacy, and parent organizations to craft the *"Nine Truths About Eating Disorders."* This document has been translated into over 30 languages and has been distributed globally to replace outdated and erroneous stereotypes about eating disorders with factual information. In this paper, we review the science behind the *Nine Truths*. **Methods:** The literature supporting each of the *Nine Truths* was reviewed, summarized, and richly annotated. **Results:** Most of the *Nine Truths* arise from well-established foundations in the scientific literature. Additional evidence is required to further substantiate some of the assertions in the document. Future investigations are needed in all areas to deepen our understanding of eating disorders, their causes, and their treatments. **Conclusions:** The *"Nine Truths About Eating Disorders"* is a guiding document to accelerate global dissemination of accurate and evidence-informed information about eating disorders.

Introduction

Eating disorders are serious mental illnesses that affect millions of individuals worldwide regardless of race, age, nationality, or sex and incur considerable personal, familial, and societal costs. The cumulative lifetime risk by age 80 of anorexia nervosa (AN), bulimia nervosa (BN) and binge-eating disorder (BED) approximates 4.6% (Hudson, Hiripi, Pope, & Kessler, 2007). Inclusion of subthreshold eating disorder behaviors raises this estimate to nearly 10%. Despite the prevalence and toll that eating disorders have on society, we lack comprehensive understanding of the etiology of eating disorders. We face significant limitations in our ability to prevent, detect, and treat this class of disorders. Stigma surrounding eating disorders has overshadowed the field for decades and has perpetuated misconceptions about their causes, hampered efforts at advancing knowledge, and misdirected lay understanding of these conditions. Perhaps most importantly, stigma surrounding eating disorders has prevented those who need help from seeking help (Ali et al., 2017).

In May 2015, the Academy for Eating Disorders (AED) and several international advocacy organizations issued a document entitled "*Nine Truths About Eating Disorders*" (http://www.aedweb.org/index.php/25-press-releases/163-press-release-aed-releases-nine-truths-about-eating-disorders?quot). The AED focused on presenting truths rather than dispelling myths to introduce empirical evidence into the general knowledge base about eating disorders. The document has been translated into over 30 languages and is being disseminated worldwide to transform perceptions and understanding of eating disorders. In this paper, we present an overview of the empirical foundation upon which the *Nine Truths* rest to foster a more accurate understanding of the current state of scientific knowledge about eating disorders for patients, families, professionals, and the public.

The truths span a broad literature. In addition to the review of empirical studies, we also attend to modern theoretical and conceptual models and authoritative reviews to evaluate the science behind the *Nine Truths*. We present several supporting statements for each truth and present a strength of evidence criteria rating for each supporting statement (Low, Moderate, or High; Supplementary Table S1). A summary is presented in Supplementary Table S2. References are presented as an annotated bibliography in supplementary online materials.

Truth #1: Many people with eating disorders look healthy, yet may be extremely ill.

1.1 Eating disorders are associated with significant medical and psychological risk

Eating disorders are associated with medical complications in multiple organ systems including the cardiovascular, gastrointestinal, musculoskeletal, dermatologic, endocrine, hematological, and neurological systems (Mehler & Brown, 2015; Mehler & Rylander, 2015; Thornton et al., 2016). The more chronic and severe the eating disorder, the greater the likelihood of serious medical complications (Westmoreland, Krantz, & Mehler, 2016). However, severe complications can emerge at any time during the course of an eating disorder (Westmoreland et al., 2016).

1.2 Most individuals with eating disorders do not appear emaciated

Weight loss is a defining characteristic of AN, but not BN or BED. In fact, eating disorders are present in all BMI categories (Duncan, Ziobrowski, & Nicol, 2017; Flament et al., 2015), and AN is less common than the combined prevalence of other eating disorder diagnoses (Kessler et al., 2013; Lindvall Dahlgren & Wisting, 2016; Qian et al., 2013). On average, the BMI of individuals with AN is lower than the BMI of those with BN, which is lower than the BMI of those with BED. Yet, restrictive eating disorders also occur among normal- and overweight individuals and individuals with BN and BED can be normal weight, overweight, or obese (see 5.4).

1.3 Somatic comorbidities of eating disorders may be difficult to detect

Many serious medical complications of eating disorders are not readily visible to lay observers or recognizable to the affected individual (see Supplementary Table S3). Even experienced healthcare professionals have difficulty accurately identifying complications or may misattribute their causes (Currin et al., 2007b; Currin, Schmidt, & Waller, 2007a; Currin, Waller, & Schmidt, 2009; Gaudiani & Mehler, 2016).

Individuals with eating disorders may fail to report the psychological components of eating disorders or have poor insight into the level of impairment associated with psychological sequelae of the disorder (Dalle Grave, Calugi, & Marchesini, 2008; Griffiths, Mond, Murray, & Touyz, 2015; Nordbø et al., 2012; Santonastaso et al., 2009; Vandereycken, 2006a; Vandereycken, 2006b). However, psychological features are often present, even if at milder levels (Carter & Bewell-Weiss, 2011) with some variation across cultures (Lee, Lee, Ngai, Lee, & Wing, 2001; Pike & Dunne, 2015)and in younger patients(Carter & Bewell-Weiss, 2011; Norris et al., 2014) (see Supplementary Table S4).

1.4 Most individuals with eating disorders do not enter treatment; those who do often do so many years into the course of illness

Epidemiological studies across the world indicate that only a minority of individuals who meet diagnostic criteria for eating disorders seek treatment (Hoek & van Hoeken, 2003; Hudson et al., 2007; Keski-Rahkonen et al., 2009; Kessler et al., 2013; Preti et al., 2009; Twomey, Baldwin, Hopfe, & Cieza, 2015). Eating disorders thus remain undetected, and, even when detected, may not be viewed as serious issues warranting medical intervention (Keel & Brown, 2010).

Truth #1: Summary and future research directions

Confidence ratings: Moderate to High (see Supplementary Table S2)

Looks may deceive, and a healthy appearance and failure to appreciate the severity of these illnesses can delay help-seeking and detection by friends, family, medical professionals, and even

patients themselves. Work is required to push past barriers to detection and care. First, longitudinal research is needed to identify early signs of medical complications and psychological comorbidities in eating disorders. A better understanding of prodromal signs and the illness trajectory will enable early detection. Understanding educational needs for physicians and other front-line providers is necessary for broad dissemination of screening and educational tools. For more information on addressing eating disorders in clinical practice, see the AED Guide to Recognition and Management of Eating Disorders (http://www.aedweb.org/index.php/education/eating-disorder-information/eating-disorder-information-13).

Truth #2: Families are not to blame, and can be the patients' and providers' best allies in treatment.

2.1 Biological risk factors contribute to the development of eating disorders

Modern etiological models of psychiatric illnesses consider the bidirectional risk between biology (see Truth #4) and environment. The assertion that parental characteristics or family dynamics are necessary and sufficient for the development of eating disorders (i.e., "families are to blame") represents an historical and dated model of psychopathology and disregards modern etiological conceptualizations of psychiatric risk. Accordingly, the first part of this truth, "families are not to blame," is empirically and logically justified. This does not imply that evaluation of family functioning in eating disorders is without merit, as such studies may provide actionable information for providers, caregivers, and patients.

2.2 Prototypical family interaction patterns that exist premorbidly among families with eating disorders have not been identified

Two critical methodological issues continue to plague studies of family functioning in eating disorders. First, most studies are correlational/differential in nature, precluding causal interpretation. Second, prospective longitudinal studies are limited, making it difficult to determine whether interactions among family members represent a cause or consequence of the illness. Some prospective studies have investigated effects of parent and family functioning in predicting later eating disorder onset with mixed results. For example, some evidence suggests that parental factors predict later eating pathology (Johnson, Cohen, Kasen, & Brook, 2002; Nicholls & Viner, 2009; Shoebridge & Gowers, 2000); however, reviews have not identified consistent patterns of risk associated with parenting styles or family interactions (Campbell & Peebles, 2014; Eisler, 2005; Larsen, Strandberg-Larsen, Micali, & Andersen, 2015; le Grange, Lock, Loeb, & Nicholls, 2010; Strober & Humphrey, 1987; Yager, 1982). Indeed, greater family conflict, reduced parental alliance, and increased feelings of depression in families with a child suffering from AN might reflect an accommodation process in response to a severe and life-threatening condition (Sim et al., 2009). Investigations of parental factors have also been limited by lack of controls with other psychiatric disorders, measurement inconsistencies, and lack of statistical power. For example, certain adverse familial experiences such as sexual abuse) may contribute to the risk of pathology in general, and are not eating disorder specific(Kendler et al., 2000).

2.3 Eating disorders place stress on families

Studies on the experience of caring for a patient with an eating disorder suggest a significant burden and negative impact on the health and well-being of caregivers—especially among mothers and partners (Anastasiadou, Medina-Pradas, Sepulveda, & Treasure, 2014; Kyriacou, Treasure, & Schmidt, 2008). Those caring for patients with AN have reported higher levels of distress than individuals caring for people with psychoses (Treasure et al., 2001). Parents initially perceive starvation as deliberate, which evokes a strong emotional response, significant distress, and can

lead to desperate responses in parents in the absence of clear guidance (Whitney et al., 2005). Attributions for these responses should consider the parent's desire to cease the starvation and to care for their child. Thus, assisting families in developing tools to deal effectively with an eating disorder is imperative. Distress associated with an eating disorder often extends beyond the identified patient. Stresses associated with having a psychiatrically ill child or partner, coupled with the responsibility for collaborating with providers in the treatment of individuals with eating disorders, underscore the importance of self-care for caregivers (Patel, Wheatcroft, Park, & Stein, 2002; Treasure & Nazar, 2016).

2.4 Family–based treatments have demonstrated effectiveness for the treatment of adolescent AN

Families are needed as patient allies during treatment (Le Grange et al., 2010). The entire family is affected when dealing with chronic and severe illnesses such as AN. Familial organizational changes that emerge may serve to maintain AN and limit access to adaptive resources the family possesses that are necessary to help overcome the eating disorder (Cook-Darzens, 2016; Eisler, 2005). Family-based treatment (FBT), whereby parents reassert control over the child's eating, is a promising approach to the treatment of adolescent AN and has some empirical support for the treatment of adolescent BN (Couturier, Kimber, & Szatmari, 2013; Le Grange, Lock, Agras, Bryson, & Jo, 2015). FBT helps families recognize and implement the resources and knowledge they possessed that predate the disorder (Lock & Le Grange, 2015). Further, FBT is recommended by many national guidelines for the treatment of eating disorders in youth (Watson & Bulik, 2013)(see Supplementary Table S5).

The role of the family is also important for adults with eating disorders. Partners can be an asset in treatment of adults since they typically express a strong desire to help, yet fear that anything they do or say will inadvertently exacerbate the situation (Treasure & Nazar, 2016).

Couple-based interventions for eating disorders leverage the power of the relationship and engage the partner in the recovery process (Bulik, Baucom, Kirby, & Pisetsky, 2011; Kirby, Runfola, Fischer, Baucom, & Bulik, 2015; Schmidt et al., 2013). Initial results of couple-based interventions are promising and suggest that close support from a family member enhances treatment regardless of patient age. However, much of family and couple-based intervention research has focused on patients with AN; additional studies are required to confirm the benefit of engaging family members in the treatment of BN and BED (see Supplementary Table S5).

Truth #2: Summary and future research directions

Confidence ratings: Low and Moderate (2.2) to High (2.1; 2.5) (see Supplementary Table S2)

In summary, typical patterns of family functioning or structure that give rise to eating disorders have not been identified. This is consistent with the AED position paper on the role of the family in eating disorders (Le Grange et al., 2010). Families are not to blame and in most cases can be the patients' and providers' best allies in treatment.

Research on family functioning has been summarized (Larsen et al., 2015; Saltzman & Liechty, 2016). These reviews point to the need for rigorous prospective designs to help understand how environmental variables, including family systems, may interact with biological risk (as discussed in Truth #7 & 8) to either heighten risk or buffer against the development of eating disorders. Eating disorders place stress on a family system, and future investigations that aim to reduce the burden on caregivers are necessary. Consideration of in-home care may be a useful direction for services. Finally, families represent an important base of support for those in recovery, and the effectiveness of family-based treatments for adolescents highlights how parents and caregivers can be important allies in treatment. Future studies that build on this success by examining how families can be best integrated into care of older adolescents, adults, and those who binge eat are of great interest.

Truth #3: An eating disorder diagnosis is a health crisis that disrupts personal and family functioning.

3.1-3.4 Eating disorders interfere with personal and family functioning

As discussed in Truth #1, an eating disorder represents a health crisis that affects every aspect of an individual's life. Signs and symptoms of an eating disorder should always be taken seriously and not dismissed or minimized. Immediate attention is warranted, and a comprehensive evaluation should be the first step in treatment planning (American Psychiatric Association, 2006; Hay et al., 2014; National Collaborating Centre for Mental Health, 2004). In addition to myriad psychiatric and medical complications and comorbidities enumerated in Truth #1, eating disorders also lead to considerable psychological distress, as well as isolation, stigmatization, and difficulties with family and other interpersonal relationships (Ali et al., 2017; Caslini et al., 2016; Dimitropoulos, McCallum, Colasanto, Freeman, & Gadalla, 2016; van Langenberg, Sawyer, Le Grange, & Hughes, 2016). Further, eating disorders are associated with financial burden (3.2), delays in healthy development (3.3), functional impairment (3.3; 3.4), and may interfere with social role functioning including intimate relationships (3.4), reproductive health (3.4) and parenting (3.4) (See summaries in Supplementary Tables S2-4).

Truth #3: Summary and future research directions

Confidence ratings: Moderate (see Supplementary Table S2)

Eating disorders clearly represent a health crisis (see Truth #1); the effects of which disrupt functioning beyond immediate complications of the eating disorder. Financial burden of eating disorders are significant, and they impact areas of social and economic well-being, along with delaying or preventing healthy childhood and adolescent development. Future investigations that examine the true cost of eating disorders over the long-term are warranted. Longitudinal studies

of eating disorders, including intervention studies, are encouraged to include secondary outcomes related to healthy development in youth, education, finances, employment, reproductive health, and overall quality of life. Further, an empirical review of the literature on relationship, role functioning, and quality of life in eating disorders would advance understanding of how eating disorders influence these vital, but understudied, outcomes.

Truth #4: Eating disorders are not choices, but serious biologically influenced illnesses.

4.1 Disordered eating behaviors can be guided by biological processes associated with automatic (unconscious) events

In vulnerable individuals, biological drives towards automaticity can provoke rigid habits to the point where individuals struggle to regain control over their dysregulated eating and physical activity (Steinglass & Walsh, 2016). For example, altered inhibitory control, the ability to refrain from engaging in prepotent automatic responses, has been shown across eating disorders subtypes (Collantoni et al., 2016; Galimberti, Martoni, Cavallini, Erzegovesi, & Bellodi, 2012) with the greatest support for bulimic-subtypes (Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016; Wu, Hartmann, Skunde, Herzog, & Friederich, 2013). Such findings are supported by a position paper that reviewed literature identifying alterations in neurobiological pathways related to reward and self-control associated with eating disorders (Wierenga et al., 2014). Further, a recent theoretical model identifies eating behaviors in AN as habitual behaviors, similar to compulsions in obsessive compulsive disorder, supported by case-control studies on neuropsychological and neuroimaging tasks (Godier et al., 2016; Steinglass & Walsh, 2016), and evidence from animal studies and human neuroimaging supports some shared neurobiology in eating disorders and other habit-related disorders, including addiction (Kaye et al., 2013b; O'Hara, Campbell, & Schmidt, 2015) .

4.2 Biologically-influenced, fundamental personality traits and cognitive styles are associated with eating disorders

Eating disorders are consistently associated with fundamental personality traits and cognitive styles. These traits are influenced by genetic factors, exist premorbidly, become exacerbated during acute stages of illness, persist after recovery, and/or may affect the prognosis of eating disorders. Some implicated traits are shared across disorders (e.g., weak central coherence, altered reward sensitivity, anxiety, difficulty with set shifting, altered interoceptive awareness), whereas others are more differentially associated with specific eating disorder phenotypes (e.g., harm avoidance in AN, negative urgency in BN; see Supplementary Table S4 for overview of associated traits). Overall, identification of genetically influenced personality and cognitive styles may reveal core biological risk factors for the development of eating disorders.

4.3 Individuals with eating disorders may experience non-typical responses to eating and activity

Individuals with eating disorders may have distinct responses to energy restriction and food consumption during an active phase of a disorder. For example, individuals with AN may have a paradoxical response to negative energy balance (i.e., taking in less energy than one expends, (Bulik, 2016), such that caloric intake is associated with dysphoric mood (Frank, 2012), whereas caloric restriction evokes a calming, anxiolytic, or euphorigenic effect (Bulik, 2016; Kaye, 2008; Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013a). Individuals with eating disorders may also experience non-typical responses to other behaviors such as physical activity and purging (Berg et al., 2013; Giel et al., 2013; Kaye, 2008; Klein et al., 2010). Such processes highlight alterations from typical experiences of reinforcement as relevant to development and maintenance of eating disorders, and such patterns may be driven by variations in neurobiology.

4.4 Eating disorders are associated with dysregulation in neurotransmitter availability and function

Although the precise underlying neurobiology is not fully understood, findings of positron emission tomography (PET) and single-photon emission computed tomography (SPECT) implicate dysregulation in both dopaminergic (DA) and serotonergic (5HT) systems in eating disorders (Culbert, Racine, & Klump, 2015; Kaye et al., 2013a; Kaye et al., 2013b; Kaye, 2008; Kessler, Hutson, Herman, & Potenza, 2016; Spies, Knudsen, Lanzenberger, & Kasper, 2015). These systems are central in rewarding aspects of food, motivation, executive functions, and the regulation of mood, satiety, and impulse control. The persistence of core eating disorder psychopathology may reflect not only preexisting neurobiological vulnerabilities, but also neuroadaptation (Treasure et al., 2015), whereby changes may occur in the brain as a consequence of prolonged eating disorder behaviors (e.g., binge eating or restriction). Adolescence, in particular, is associated with a host of neuronal changes, such as increased synaptogenesis, pruning, and myelination of frontal and limbic areas, which are involved in emotional processing and cognition (Benes, 1998; Blakemore & Choudhury, 2006; Tau & Peterson, 2010). A maturing brain may be particularly vulnerable to the insults caused by extreme food restriction or excessive exercise resulting in negative energy balance or highly variable energy consumption (binge-fast cycles).

4.5 Brain structure and function differ between those with active eating disorders and healthy individuals

Both human and animal studies have addressed the role of brain anatomy and function in eating disorder psychopathology through use of brain imaging techniques. Studies have revealed deviations in structure, function, and activation in the brains of individuals with eating disorders, and are reviewed comprehensively in several publications (Frank, 2013; Frank, 2015a; Kaye,

2008; O'Hara et al., 2015; Seitz et al., 2014; Seitz, Herpertz-Dahlmann, & Konrad, 2016; Titova, Hjorth, Schiöth, & Brooks, 2013; Van den Eynde et al., 2012).

Structural neuroimaging studies in eating disorders have predominantly shown grey matter reductions in various brain regions that are most pronounced in patients with AN (Seitz et al., 2016). Associations with nutritional abnormalities have been repeatedly demonstrated and in AN volume reductions tend to quickly normalize with weight gain (Bernardoni et al., 2016; Seitz et al., 2016). Functional and structural neuroimaging studies in eating disorders provide evidence that aberrant frontostriatal neural circuitry may represent altered reward pathways, manifesting in impaired regulation of appetite, emotion, and self-control (Frank, 2015b; Friederich, Wu, Simon, & Herzog, 2013; Kaye, Wagner, Fudge, & Paulus, 2011; Kessler et al., 2016; Marsh et al., 2009; Marsh, Maia, & Peterson, 2009). Specifically, altered functioning of limbic regions together with either reduced or exaggerated 'top-down' cognitive control (via the prefrontal cortex) are seen as contributing to impulsive (e.g., BN, BED) or exaggerated self-control (e.g., AN) related symptoms/behaviors (Ehrlich et al., 2015; Friederich et al., 2013; Hege et al., 2015; Kaye & Strober, 2009; Kessler et al., 2016; King et al., 2016; Marsh et al., 2009; Sanders et al., 2015). Neuroimaging and behavioral findings suggestive of alterations in reward pathways has been shown across eating disorders [see(Frank, 2015a) for review]. Findings are mixed regarding the direction of change and the subregions of the brain reward system, likely due to research design issues such as failure to control for nutritional and medication status, exercise, comorbidity, and inadequate sample sizes (Frank, 2015a).

Evidence from brain structure and function, though preliminary, advances support for the assertion that eating disorders are biologically influenced. Brain structure and function appears to be altered in the active disease state, though the exact nature and stability of differences requires further investigation. Even if brain structure and function differences only occur after an initial

shift in eating behavior, these changes may highlight biologically-driven maintenance patterns that impede recovery.

4.6 Feeding and activity behavior is biologically regulated in animals

Animal models shed light on highly specific brain pathways implicated in eating disorder features, including restriction and binge eating. Controlled experiments have led to the development of animal models of hunger (Atasoy, Betley, Su, & Sternson, 2012) and binge eating (Murray, Tulloch, Chen, & Avena, 2015), providing evidence of neurobiological origins of eating disorders. In addition, an activity-based anorexia rodent model [e.g., (Chowdhury, Chen, & Aoki, 2015)] highlights increased physical activity and reduced body weight in response to restricted food access in animals. Using neural circuit-level approaches that enable activation or inhibition of anatomically and genetically defined brain pathways, like optogenetics and chemogenetics, multiple pathways have been identified that regulate different patterns of feeding behavior (Hardaway, Crowley, Bulik, & Kash, 2015; Sternson & Roth, 2014); see Supplementary Table S7 for specific regions and nuclei). This approach elevates understanding of how discrete neural circuits control feeding and metabolism, and provides additional evidence of how feeding behavior may be biologically influenced. Further study is needed to determine whether these are therapeutic entry points into pathological models of eating disorders.

4.7 Endocrine changes are associated with eating disorder risk

The risk for eating disorders increases during reproductive milestones (e.g., puberty, pregnancy) and sex hormones play a role in this risk (Baker, Girdler, & Bulik, 2012; Klump, Keel, Sisk, & Burt, 2010). For example, AN in females typically develops around puberty and is rare before the pubertal transition. Earlier pubertal timing is also associated with increased eating disorder symptoms. Increases in estrogen at puberty are hypothesized to activate genes that influence eating disorder development (Culbert et al., 2015; Culbert, Racine, & Klump, 2016; Klump et al., 2010).

The increased risk for eating disorder symptoms at puberty is not surprising given that puberty in females involves considerable changes not only in sex hormones, but also in body composition and in neuropeptides that modulate metabolism (Loomba-Albrecht & Styne, 2009; Siervogel et al., 2003).

Pregnancy has also been suggested as both a risk and protective period for eating disorder symptoms. Women with acute AN and BN often report symptom improvement or remission during pregnancy, whereas pregnancy increases risk for relapse for those in remission from AN (Kimmel, Ferguson, Zerwas, Bulik, & Meltzer-Brody, 2016). Pregnancy may also mark a vulnerable time for BED onset (Bulik et al., 2007). Eating disorder symptoms fluctuate across the menstrual cycle in a manner that mirrors changes in sex hormones (Baker et al., 2012; Edler, Lipson, & Keel, 2007; Klump, Keel, Culbert, & Edler, 2008; Racine et al., 2012). Paralleling these findings, a direct association between diminishing estrogen and increasing progesterone levels and eating disorder symptoms has been observed (Edler et al., 2007; Klump et al., 2008). The menopause transition, which involves prolonged and erratic changes in sex hormones, may represent an additional vulnerability period for the development or re-emergence of an eating disorder (Baker & Runfola, 2016; Mangweth-Matzek et al., 2013).

Much less is known about the role of reproductive milestones and sex hormones in the risk for eating disorders in males. Some studies suggest that boys who experience either early or late puberty are at increased risk for eating disorder symptoms (Ricciardelli & McCabe, 2004). Testosterone may be a protective factor against eating disorder development, but findings are mixed and additional investigation is warranted (Baker et al., 2012).

In addition, aberrant blood and cerebrospinal fluid levels of various appetite-regulating peptides have been observed in individuals suffering from AN or BN (Monteleone & Maj, 2013). Most of these studies, however, are limited both by small sample sizes and their sampling process

because plasma levels of appetite-regulating peptides may not reflect the concentrations in the central nervous system. Serum leptin levels have also been tied with eating disturbances. Serum leptin levels correspond with fat mass in healthy, energy-balanced humans (Hebebrand, Muller, Holtkamp, & Herpertz-Dahlmann, 2007). As would be expected due to their low BMI and fat mass, in acute stages of the illness, individuals with AN generally have low serum leptin levels (Föcker et al., 2011). The observed levels in AN are typically lower than those in BMI-matched healthy lean individuals, most likely due to differences in fat mass (Hebebrand et al., 2007). Intriguingly, hypoleptinemia in AN has also been associated with characteristic hyperactivity (Ehrlich et al., 2009; Holtkamp et al., 2006). Hypoleptinemia is considered to be a state biomarker for AN and together with BMI may represent a useful diagnostic test to distinguish constitutional thinness from AN (Föcker et al., 2011). Many additional endocrine changes are observed in eating disorders (see Supplementary Table S3).

Truth #4: Summary and future research directions

Confidence ratings: Moderate to High (see Supplementary Table S2)

The precise nature of underlying biological signatures is an active area of investigation and evidence in support of Truth #4 is accumulating rapidly. In-depth work concentrating on personality traits, cognition, neurobiology, brain anatomy and function, endocrinology, genomics and other -omics (see Truths #7 and 8) contributes to improved understanding of the biological underpinnings of eating disorders. Future research directions for this truth include: 1) examining neuropsychologically-based treatment approaches and outcomes; 2) treatment matching based on phenotypic psychobiological profiles; 3) evaluation of childhood behavioral and neurobiological traits; 4) systematic reviews on altered response to food and exercise in eating disorders and brain function; 5) additional investigation of neurotransmitter availability and function in eating

disorders using methods including postmortem brain analyses, measures of cerebrospinal fluid, PET imaging, and magnetic imaging spectroscopy; 6) basic science and animal research to further probe neural circuitry associated with eating disorder risk; and 7) further examination of the role of longitudinal endocrine changes in eating disorders, including the menopause transition along with the role of hormonal changes in men's eating risk.

Truth #5: Eating disorders affect people of all genders, ages, races, ethnicities, body shapes and weights, sexual orientations, and socioeconomic statuses.

5.1 Eating disorders affect both males and females

Since research on eating disorders has historically focused on women, the nosology of eating disorders has evolved based on female symptom profiles (Anderson & Bulik, 2004) and normative data on males are lacking (see Supplementary Figure S1 for lifetime prevalence of eating disorders by sex). Available evidence suggests that males may also be less likely to seek treatment (Striegel, Bedrosian, Wang, & Schwartz, 2012), less likely to be diagnosed with an eating disorder even when presenting with identical symptoms as females (Currin et al., 2007a), and less likely to access treatment even with similar clinical severity (Austin et al., 2008).

5.2 Eating disorders occur across the lifespan

The typical age of onset of both AN and BN is in adolescence or early adulthood (Currin, Schmidt, Treasure, & Jick, 2005; Keski-Rahkonen et al., 2007; Keski-Rahkonen et al., 2009; Smink, van Hoeken, & Hoek, 2012; Zerwas et al., 2015). Childhood-onset AN is seen clinically from about age 7 years upwards, whereas BN before puberty is quite rare (Nicholls & Bryant-Waugh, 2009). Likewise, BED often begins in late adolescence or early adulthood (Hudson et al., 2007; Kessler et al., 2013; Mustelin, Raevuori, Hoek, Kaprio, & Keski-Rahkonen, 2015; Preti et al., 2009), though some people report that they began binge eating early in life (around age 11 years)—even

before going on their first diet (Grilo & Masheb, 2000). Overall, however, BED commonly begins later than AN and BN, with new cases steadily arising up to age 40-60 years in the population (Hudson et al., 2007; Preti et al., 2009).

Eating disorders in midlife are either recurring or persisting earlier-onset disorders or new late-onset disorders (Baker & Runfola, 2016; Gagne et al., 2012; Peat, Peyerl, & Muehlenkamp, 2008). Bulimic symptoms in particular are relatively common in midlife women (Baker et al., 2017; Gagne et al., 2012), with one study finding that, among 2,000 women above age 50, 13% endorsed an eating disorder symptom (Gagne et al., 2012). Although the etiology of midlife eating disorders remains poorly understood, life events such as divorce, loss of family members, or somatic illness could serve as triggers (Kally & Cumella, 2008; Peat et al., 2008), and pregnancy or menopause with accompanying biological changes may increase vulnerability for onset or recurrence of eating disorders (Baker & Runfola, 2016; Baker et al., 2017; Bulik et al., 2007; Peat et al., 2008). Very little is known about eating disorders in men in midlife and beyond.

5.3 Eating disorders occur in all races and ethnicities

A review of community studies from 30 countries found no systematic association between ethnicity/race and eating disorder occurrence (Mitchison & Hay, 2014). Although eating disorders were initially considered to be limited to Western culture, accumulating evidence ties eating disorders more generally to economic development, urbanization, and industrialization across the globe (Pike, Dunne, & Addai, 2013; Pike, Hoek, & Dunne, 2014). Rising incidences of eating disorders have been reported in numerous countries, particularly in Asia and the Middle East (see Supplementary Figure S2) (Pike & Dunne, 2015; Pike et al., 2014). In the United States, the prevalence of eating disorders in ethnic and racial minority groups is similar to non-Latino whites, while ethnic minority groups more frequently report binge-eating behavior as compared to non-Latino whites (Marques et al., 2011). AN was found to be somewhat less common among Black

than White Americans (Pike et al., 2013; Striegel-Moore & Franko, 2003). Importantly, racial and ethnic minorities are underrepresented in specialist eating disorder services, possibly due to underdetection in primary care (Striegel-Moore et al., 2003).

5.4 Eating disorders occur in individuals of all shapes and sizes

Weight and BMI can vary substantially across the different types of eating disorders. In a sample of over 3,000 adolescents, eating disorders were present in all BMI categories (Flament et al., 2015). Restrictive eating disorders in normal- and overweight individuals are increasingly being acknowledged. The DSM-5 facilitates the diagnosis of atypical AN in individuals who meet all criteria for AN with the exception of low weight (American Psychiatric Association, 2013). This diagnosis is appropriate, for example, in individuals who begin at high weights and lose weight precipitously. A substantial portion of treatment-seeking adolescents with restrictive eating disorders have a history of overweight or obesity (Lebow, Sim, & Kransdorf, 2015), and there is a well-established relationship among dietary restriction, obesity, and eating disorders (Field et al., 2003; Neumark-Sztainer et al., 2006). In a review of clinical trials of BN, baseline BMI was most commonly in the normal range (Berkman et al., 2006), whereas community studies indicate that BN is prevalent in overweight and obese adolescents (Flament et al., 2015) and predicts weight gain over time (Fairburn, Cooper, Doll, Norman, & O'Connor, 2000; Micali et al., 2015). Individuals with BED are commonly overweight or obese (Hudson et al., 2007; Kessler et al., 2013), yet a substantial minority of individuals with BED are normal-weight, particularly early in the course of illness (Fairburn et al., 2000; Mustelin et al., 2015).

5.5 Eating disorders are present across different sexual orientations and gender identities

Homosexual orientation is regarded as a risk factor for eating disorders in men: gay and bisexual men report more body dissatisfaction and disordered eating, and are more likely to be diagnosed with an eating disorder than heterosexual men (Brown & Keel, 2012; French, Story, Remafedi,

Resnick, & Blum, 1996; Russell & Keel, 2002). In women, the evidence on sexual orientation and disordered eating is mixed. Lower body dissatisfaction among homosexual and trans women have been observed in some, but not all studies (Alvy, 2013; French et al., 1996; Moore & Keel, 2003; Morrison, Morrison, & Sager, 2004; Witcomb et al., 2015). In a population-based cohort of adolescents, unhealthy weight control behaviors (e.g., laxative use, fasting, and vomiting) were significantly more prevalent among sexual minority males and females than in their heterosexual peers (Hadland, Austin, Goodenow, & Calzo, 2014).

Most research on eating-related pathology has focused on cisgender individuals (i.e., those whose gender identity matches the sex they were assigned at birth). A study of over 280,000 American college students indicated that transgender individuals may be the sexual minority with the highest eating disorder risk: 16% of transgender youth reported being diagnosed with an eating disorder in the past year, compared with 2% and 4% of cisgender sexual minority men and women, respectively (Diemer, Grant, Munn-Chernoff, Patterson, & Duncan, 2015). Similarly, a study of Canadian transgender youth and of UK transgender adults found high rates of endorsement of disordered eating behaviors particularly among trans males (Watson, Veale, & Saewyc, 2016; Witcomb et al., 2015).

5.6 There is no consistent association between socioeconomic status and risk for eating disorders

Although higher parental education has been associated with increased risk of being diagnosed with an eating disorder in registry studies (Ahrén et al., 2013; Goodman, Heshmati, & Koupil, 2014), evidence suggests that this association may be genetically rather than socially mediated (Duncan et al., 2017). No consistent association has been observed between socioeconomic status and risk of eating disorders (Mitchison & Hay, 2014). In Australian population surveys, both binge eating and purging increased more in low-income than high-income individuals during a 10-year

time period, suggesting an ongoing shift in the demographics of disordered eating (Mitchison, Hay, Slewa-Younan, & Mond, 2014).

Truth #5: Summary and future research directions

Confidence ratings: Moderate to High (See Supplementary Table S2)

In summary, no dominant pattern of age, body size, sexual orientation or gender identity, race, ethnicity, or socioeconomic status is associated with eating disorder risk. Providers should remain vigilant to eating disorders in all individuals regardless of demographic characteristics.

Longitudinal studies that consider weight trajectories as they relate to eating disorder symptom development are needed, as it is clear that individuals may develop eating disorders from any premorbid weight. More research on eating disorders among sexual minorities is also necessary for the development of targeted prevention and intervention efforts, specifically longitudinal studies that examine how sexual and gender identity development in youth may impact eating disorder risk.

Truth #6: Eating disorders carry an increased risk for both suicide and medical complications.

6.1 Eating disorders are associated with premature death

The most significant medical complication of an eating disorder is premature death. The standardized mortality ratio (SMR) associated with AN ranges between 5.9 and 6.2, meaning the risk of death for individuals with AN is up to 6.2 times greater than the risk in the general population, and the weighted annual mortality rate of AN is reported as 5.1 per 1000 person years (Chesney, Goodwin, & Fazel, 2014; Papadopoulos, Ekbom, Brandt, & Ekselius, 2009). Additionally, mortality in AN is 12 times higher than the annual all-cause mortality rate in females 15-24 years old from the general population (Klump, Bulik, Kaye, Treasure, & Tyson, 2009).

Notably, AN also has one of the highest mortality rates of any psychiatric illness (Chesney et al., 2014), and one in five deaths in AN is attributable to suicide (Arcelus, Mitchell, Wales, & Nielsen, 2011).

The mortality rate for BN is also significantly elevated relative to the general population, with meta-analyses estimating the SMR for BN to be 1.9 (Chesney et al., 2014). One clinical follow-up study in Finland found the all-cause mortality hazard ratio for BED to be 1.77 (0.60, 5.27) (Suokas et al., 2013). Though similar in effect size to reported SMRs for BN, this hazard ratio for BED was not significant. For those with BN, mortality risk may increase with severity (Huas et al., 2013). With the inclusion of BED in the DSM-5, more studies on epidemiology, course, and outcome of BED are likely.

6.2 Risk of suicide is elevated in eating disorders

The risk of suicide attempts is also elevated in eating disorders. In the Swedish population born between 1979 and 2001, the odds ratio (OR) of suicide attempts was estimated to be 5.3 (95% CI: 5.0, 5.5) for any eating disorder, meaning that the risk of suicide attempts in people with eating disorders is 5.3 times the risk in individuals without an eating disorder (Yao et al., 2016). The ORs for suicide were 4.4 (95% CI: 4.1, 4.7) for AN and 6.3 (95% CI: 5.7, 6.9) for BN (Yao et al., 2016). Similar relative risks have been reported in the Danish population (1989-2006) (Zerwas et al., 2015). A large clinical study found that 35.6% of eating disorder patients had attempted suicide at least once (Fedorowicz et al., 2007), and patients with binge eating and/or purging behaviors were associated with an elevated risk for suicide attempts compared with patients without such behaviors (Fedorowicz et al., 2007; Foulon et al., 2007). In Sweden, 13.6% of women with a lifetime history of BED had at least one lifetime suicide attempt (Pisetsky, Thornton, Lichtenstein, Pedersen, & Bulik, 2013; Runfola, Thornton, Pisetsky, Bulik, & Birgegård, 2014).

Based on a meta-analysis, the *suicide-specific* SMR is 18.1 (11.5, 28.7) for AN (Keshaviah et al., 2014). Among female AN patients in specialized care, this ratio could be as high as 31.0 (21.0, 44.0) (Preti, Rocchi, Sisti, Camboni, & Miotto, 2011). The suicide-specific SMR is reported as 7.5 (1.6, 11.6) for BN (Preti et al., 2011) and no deaths by suicide in individuals with BED were reported; however, more data for BED are expected to emerge as recognition and reporting of BED increases. Familial co-aggregation of eating disorders and suicide attempt has been observed in nationwide population data (Yao et al., 2016). Two studies from Australia (Wade, Fairweather-Schmidt, Zhu, & Martin, 2015) and Sweden (Thornton, Welch, Munn-Chernoff, Lichtenstein, & Bulik, 2016) have reported that the co-occurrence of eating disorders and suicide may be in part due to shared genetic factors.

Whereas women with disordered eating in the community may be more likely to attempt suicide than males (Davison, Marshall-Fabien, & Gondara, 2014), no sex differences have been found for the risk of suicide attempts or death by suicide in eating disorders (Yao et al., 2016).

Truth #6: Summary and future research directions

Confidence ratings: High (see Supplementary Table S2)

Increased risk of premature death, including suicide, among eating disorders is well established; however, little is known about the mechanism underlying this association. Future investigations should consider why eating disorders specifically display increased risk for suicide and examine how psychobiological models of suicide [e.g. (Anestis et al., 2016)] may pertain to those with eating disorders, including how unique complications associated with eating disorders, such as nutritional status, may influence risk as proposed by these models.

Truth #7: Genes and environment play important roles in the development of eating disorders.

7.1 Eating disorders run in families

Family, twin, and genetic research has established that eating disorders run in families and genes play a role in this familial pattern (Yilmaz, Hardaway, & Bulik, 2015). Familial history of AN increases the risk of AN development fourfold compared with the general population (Steinhausen, Jakobsen, Helenius, Munk-Jørgensen, & Strober, 2015). Furthermore, AN, BN, and eating disorder not otherwise specified (EDNOS) track together in families, suggesting a lack of specificity (Lilenfeld et al., 1998; Strober, Freeman, Lampert, Diamond, & Kaye, 2000). BED also aggregates in families independent of obesity (Fowler & Bulik, 1997; Hudson et al., 2006). Twin studies cannot identify which genes influence risk, but they have identified a strong genetic contribution in AN, BN, and BED. Specifically, 48-74% of the total variance in liability to AN, 55-62% to BN, and 39-45% to BED is attributable to genetic factors (Yilmaz et al., 2015).

7.2 Genes play a role in eating disorder risk

Genome-wide association studies (GWAS), which scan the entire genome in a hypothesis-free manner, and related approaches such as exome sequencing and whole genome sequencing have rapidly accelerated the field. The Eating Disorders Working Group of the Psychiatric Genomics Consortium recently identified the first genome-wide significant locus for AN (Duncan et al., 2017) in an area that harbors genes previously implicated in type 1 diabetes and other autoimmune disorders. We expect this will mark an inflection point in genomic discovery if AN follows the same progression of findings as other psychiatric disorders such as schizophrenia, where increased sample size has led to fruitful genomic discovery (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). GWAS represents a starting point for genomic discovery, as post-GWAS science reveals causative biological pathways and the functional significance of implicated genes and epigenetic enhancer regions. No GWAS of BN or BED have been conducted to date. In addition to GWAS approaches, familial linkage analysis with whole-genome and exome

sequencing has identified two missense potential mutations (Cui et al., 2013), which evidence a connection with eating-disordered behaviors in a recent mouse model (Lutter et al., 2016).

7.3 Environmental factors play a role in eating disorder risk

Genes do not act alone: environment plays an important role. Cross-sectional and longitudinal twin studies also indicate that nonshared environmental factors account for variance in eating disorder symptoms. Cultural pressure for thinness has been identified as a specific risk factor for eating disorders, and clinical trials of interventions that reduce thin-ideal internalization have led to reductions in eating disorder symptoms [see (Culbert et al., 2015)]. While thin-ideal internalization may have some genetic influence, one longitudinal twin study indicates that nonshared environmental influences were most important in the etiology of thin-ideal internalization (Suisman et al., 2014).

7.4 Only a small portion of individuals exposed to environmental risk develop eating disorders

Dieting, drive for thinness, and portion size escalation are widespread in industrialized countries and may represent risk scenarios for the development of eating disorders (Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004; Steenhuis & Vermeer, 2009; Striegel-Moore & Bulik, 2007); however, despite nearly ubiquitous exposure, threshold illnesses are disproportionately rare. A current hypothesis is that individuals *genetically predisposed* to eating disorders are most vulnerable to societal pressures and environmental insults. Eating disorders are "complex traits," meaning that multiple genetic and environmental factors—each of small to moderate effect— act together to increase risk. Genetic and environmental factors may not only act in an additive manner, but may co-act in other ways (see Truth #8).

Truth #7 – Summary and future research directions

Confidence rating: Moderate to High

Genomic discovery in AN is accelerating rapidly, but work on BN and BED is woefully behind. Very large sample sizes (in the tens of thousands) are key to discovering genetic variants associated with risk, and global cooperation is underway to achieve such sample sizes. Advances in genetic methodology, coupled with increasing knowledge about environmental risk factors, will provide a more complete and accurate picture of eating disorder etiology.

Truth #8: Genes alone do not predict who will develop eating disorders.

8.1 Eating disorders do not follow Mendelian transmission patterns

Inheritance patterns for eating disorders do not follow the traditional Mendelian patterns where variation in one gene results in one disorder (e.g., Huntington's chorea). Rather, hundreds (or perhaps thousands) of genes act in concert and are influenced by environmental factors. An individual's risk is a composite of the cumulative number of genetic and environmental risk and protective factors to which they are exposed.

8.2 Many cases of eating disorders are sporadic, meaning there is no known family member who suffers from an eating disorder.

Family studies indicate that the relative risk for eating disorders is higher in family members of affected individuals; however, the majority of affected individuals have no known affected family members (Bould et al., 2015; Steinhausen et al., 2015; Strober et al., 2000). This literature is limited in that eating disorder history among relatives may not be fully known or accurately captured.

8.3 Genes and environment may co-act to influence risk for eating disorders

For eating disorders, as in all complex traits, genes represent probabilities. Individuals with a high genetic susceptibility for disordered eating may be protected by other factors, whereas individuals who are at relatively low genetic risk may be burdened with cumulative or extreme environmental insults such that they develop eating disorders despite their favorable genetic profile. Understanding the role that genes and environment play in eating disorders requires a deep acceptance of probability and of uncertainty.

Genes and environment may co-act to influence risk for eating disorders (Trace, Baker, Peñas-Lledó, & Bulik, 2013). First, in most families, parents and extended family provide both genes and shared environment, meaning that these two factors are confounded. Second, individuals with a stronger genetic susceptibility for eating disorders might be more sensitive to environmental factors (dieting, bullying, teasing, or overeating). Whereas many adolescents may try dieting, only for a few does it serve as an environmental trigger for an underlying genetic predisposition. Third, an individual who is genetically predisposed to traits associated with eating disorders (i.e., perfectionism, persistence, high physical activity) can seek out environments that may serve as triggers (e.g., sports that have a lean body type ideal, certain social media content) (Carrotte, Vella, & Lim, 2015; Giel et al., 2016; Rousselet et al., 2017). This interaction is known as an active gene-environment correlation (Plomin, DeFries, & Loehlin, 1977) Genetic research combined with ambulatory assessment may help understand how environmental influences affect risk for eating disorders by pinpointing specificity of risk factors.

Rigorous studies of gene-environment interaction in eating disorders are sparse. Some developmental twin studies have examined gene-environment interaction (Culbert et al., 2015). For example, contribution of genetic risk to the emergence of dysfunctional eating attitudes and disordered eating varies with developmental stage, with higher genetic effects observed in mid-to-late adolescence and mid-to-late puberty (Culbert et al., 2015; Culbert, Burt, McGue, Iacono, &

Klump, 2009; Klump, Burt, McGue, & Iacono, 2007). More sophisticated analytic techniques that examine *interplay* between genetic risk and family environment provide indication that fit between an individual's genotype and their family environment may be relevant for eating disorder risk (Culbert et al., 2015). In human studies, large samples using genome-wide and phenome-wide data are required for credible conclusions. Following a report of a rare missense mutation being associated with the development of eating disorders, Lutter et al. (2016) found that group (vs. individually) housed transgenic female mice displayed irregular feeding and anxiety behaviors (Lutter et al., 2016) preliminarily revealing both sex-specific and gene by environment effects.

Additional ways in which genes and environment interact are via mechanisms collectively called epigenetics—the modification of DNA, RNA, or proteins by biological or environmental factors. These mechanisms alter gene expression without changing the DNA sequence. Importantly, epigenetic changes such as DNA methylation are tissue specific and can rarely be directly studied in the brain. Therefore, it is important to determine whether epigenetic changes seen in blood are good proxies for epigenetic changes in brain (Walton et al., 2016).

Preliminary epigenetic studies have reported changes in dopaminergic genes and genes for proopiomelancortin (*POMC*), cannabinoid receptor 1 (*CNR1*, also referred to as *CB1*), atrial natriuretic peptide (*NPPA*, also referred to as *ANP*), alpha synuclein (*SNCA*), and oxytocin receptor (*OXTR*) (Ehrlich et al., 2010; Ehrlich et al., 2012; Frieling et al., 2007; Frieling et al., 2008; Frieling et al., 2010; Kim, Kim, Kim, & Treasure, 2014; Schroeder et al., 2012). If replicated, epigenetic findings could make important contributions to understanding the role of of non-DNA elements in eating disorder susceptibility.

Truth #8: Conclusions and future research directions

Confidence ratings: Low to High (See Supplementary Table S2)

A complex interplay between genetic and environmental factors underlies the development of eating disorders. Future research on genetic pathways and their interplay with environmental factors is an exciting and emerging area of research—and one that has the potential to provide key understanding of the multiple and nuanced facets by which individuals may develop eating pathology. In the short-term, large population-based studies with both genotypic and phenotypic information to probe gene-environment interactions, along with case-control studies to examine potential epigenetic effects represent key areas for advancing knowledge regarding complex risk patterns.

9. Truth #9: Full recovery from an eating disorder is possible. Early detection and intervention are important.

9.1 A substantial portion of individuals with eating disorders achieve recovery

Full recovery from an eating disorder is not only possible, but indeed probable. A substantial portion of individuals with eating disorders achieve recovery, some without seeking treatment (Eddy et al., 2016; Keel & Brown, 2010; Steinhausen & Weber, 2009; Steinhausen, 2009). Five-year clinical recovery rates have been estimated at 67% for AN (Keski-Rahkonen et al., 2007) and 55% for BN (Keski-Rahkonen et al., 2009) in community samples, and by 10 years after eating disorder onset 70% of individuals are recovered (Berkman, Lohr, & Bulik, 2007). Although recovery is attainable, there is a lack of consensus on the exact definition of recovery, making it difficult to compare recovery rates across studies (Bardone-Cone et al., 2010; Emanuelli, Waller, Jones-Chester, & Ostuzzi, 2012). Traditionally, these definitions focus on physical and behavioral recovery. Physical recovery refers to the resumption and maintenance of a healthy body weight and a normalization of all physical parameters affected by the eating disorder, whereas behavioral recovery means the absence of eating-disorder related behaviors such as food restriction, binge eating, and purging. Psychological recovery, including the attainment of normal attitudes toward

food and the body, is important yet often overlooked. It has been proposed that full recovery is achieved only when patients are indistinguishable from healthy controls on all eating disorder related measures, including psychological aspects (Bardone-Cone et al., 2010). Although this definition may seem stringent, it is attainable. Full recovery from an eating disorder is possible, and given that lingering eating disorder attitudes predict relapse (Helverskov et al., 2010), the psychological component of recovery is clinically relevant.

9.2 Early detection and intervention may improve prognosis

For some, recovery from an eating disorder is possible without treatment; however, early detection and intervention are preferred for all eating disorders (Treasure et al., 2015). For AN, a longer duration of illness before presentation for treatment is associated with poor outcome (Keel & Brown, 2010; Pike, 1998; Richard, Bauer, & Kordy, 2005), and the probability of recovering decreases as a function of duration of illness, irrespective of treatment (Pike, 1998). For BN, some studies find that a longer duration of illness is associated with poor outcome, whereas others observe that severity of illness and additional psychiatric comorbidities are more significant predictors of outcome (Steinhausen & Weber, 2009). However, in general, the sooner an eating disorder is identified and treatment can begin, the better prognosis there is for full recovery.

9.3 Effective psychological interventions for eating disorders exist. Many, but not all, patients benefit & 9.4 Medication can be an effective treatment component for eating disorders

Treatment for an eating disorder typically includes psychological treatment and may include medication (Zipfel, Giel, Bulik, Hay, & Schmidt, 2015). For AN, weight restoration is an essential first step in treatment. Inpatient renourishment for AN is typically directed by clinical guidelines that advocate for a "low and slow" approach, due to concerns about refeeding syndrome (Solomon & Kirby, 1990). However, this approach is being challenged in favor of more aggressive renourishment techniques, leading to shorter hospital stays and a favorable safety profile (Garber

et al., 2013; Madden et al., 2015; Redgrave et al., 2015). Once medical stabilization of an eating disorder is established, patients may step down to other levels of care. The evidence base has been thoroughly reviewed for psychotherapeutic and medication interventions for eating disorders. Supplementary Tables S5 & S6 provide an overview of psychotherapeutic and medication treatments.

Truth #9: Summary and future research directions

Confidence Ratings: Low to High (See Supplementary Table S2)

Increasing understanding of the underlying mechanisms of eating disorders will facilitate the development of more effective and personalized prevention and treatment options, eventually leading to increased recovery rates and shorter recovery times. Some evidence-based treatments have proven efficacy. Importantly, recovery from eating disorders can and does occur at any age and for those who do not achieve complete remission, quality of life and somatic status may be improved, monitored, and stabilized (Treasure, Stein, & Maguire, 2015). Future research goals include development of strategies for early detection and intervention, development of a provider's toolbox that includes psychological and pharmacological interventions that are effective for a range of eating disorders in diverse populations, drug development or repurposing investigations to target core biological pathology of AN, studies of long-term efficacy of medication interventions for all eating disorders, and studies of the effectiveness of medications for eating disorders in community settings.

General Conclusion

We summarize the available literature that led to the development of the "*Nine Truths About Eating Disorders."* Eating disorders are not choices and do affect individuals from all walks of life. They result from a combination of biology, genetics, and environment. Eating disorders increase the

risk for suicide and medical complications, and interrupt personal and family functioning. Families are not to blame and can be critical sources of support in recovery.

Clearly, additional work is needed to better understand risk factors, course of illness, and treatment of eating disorders. Important for advancing science in this area is the ability to remain flexible in thinking about causal factors and acknowledge accumulating evidence underlying these truths to eliminate misconceptions that have plagued the field for decades. In addition, providers should be mindful of the multitude of ways eating disorders can arise and be especially vigilant to signs of medical and psychiatric complications resulting from AN, BN, and BED. As scientists, providers, patients, family, and friends, we need to continue educating others in the community about these truths in order to detect and treat eating disorders as soon as possible.

Yet, the science of this field cannot be advanced in the absence of appropriate investment and financial support from organizations worldwide that fund research. A 2015 blog post by the former director of the US National Institute of Mental Health, Thomas Insel, MD, revealed how woefully underfunded research on eating disorders was relative to the disability-adjusted life years associated with the illnesses (http://www.nimh.nih.gov/funding/funding-strategy-for-research-grants/white-paper_149362.pdf). Despite the dire morbidity and mortality statistics, eating disorders continue to be low-priority illnesses, we contend, in part due to long-standing misconceptions about their causes and consequences. Funding is required for larger more definitive collaborative studies to avoid the confusion that arises from conflicting results from small, underfunded, underpowered, and unreplicated investigations. Far too often, such small-budget studies are all that investigators can afford to conduct.

Science is constantly evolving, and novel methods will enhance our ability to clarify the etiology of eating disorders and to develop scientifically informed and effective treatments for these debilitating illnesses. With adequate support for science, emerging information will facilitate

the refinement of the *Nine Truths* and may in fact uncover new truths. Ultimately, it is our hope that dissemination of the *Nine Truths* will serve to reduce stigma and misunderstanding, and, via their impact on science and practice, reduce illness burden, improve quality of life, and eliminate mortality from eating disorders.